12th International Congress on Drug Therapy in HIV Infection

Gender Differences in the Use of Cardiovascular Disease-related Interventions Among HIV-positive Persons: D:A:D Study

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On behalf of the D:A:D Study group

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REGION H

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D:A:D

Background

- There have been substantial reductions in the incidence of myocardial infarction (MI) and improvements in post-MI survival in the general population
- Improvements have tended to lag in women compared to men[1,2]
- Reasons for this gender difference remain unclear – possibly partly explained by less use of some drug interventions, less use of invasive cardiovascular procedures (ICPs)[2,3], and less monitoring of risk factors in women
- Lack of data on potential gender differences in the use of interventions to prevent and treat cardiovascular disease (CVD) in HIV-positive individuals

1.C Koopmana et.al *Int J Cardiol. 2013; 168:993–8.* 2. R Pelletier et.al *CMAJ. 2014;186:497–504*.
3. DM Bell et. al *Pharmacotherapy. 2000;20:1034–44.*

Study Aim

- To investigate whether gender differences exist in the use of CVD-related interventions in the D:A:D Study

- CVD-related interventions of interest:
  - Lipid lowering drugs (LLDs)
  - Angiotensin Converting Enzyme Inhibitors (ACEIs)
  - Anti-hypertensives
  - Invasive Cardiovascular Procedures (ICPs):

    -Angioplasties, bypasses, carotid endarterectomies

Methods

- Observational study of >49,000 HIV-positive persons from 11 cohorts across Europe, Australia and USA
- D:A:D primary aim: To investigate potential associations between the use of antiretroviral drugs (ARVs) and CVD (incl. MIs, strokes and ICPs) and other clinical events

- Data are collected prospectively:
    - Socio-demographic factors
    - Use of ARVs
    - Various HIV and laboratory markers
    - CVD-related risk factors and drugs
    - Incident MIs/strokes and ICPs, centrally validated

Statistical Methods

- Follow-up from 01/02/99 until the earliest of death, six months after last visit or 01/02/13
- Individuals with MI/stroke at baseline excluded
- Rates of initiation of CVD-related interventions were calculated for the total time of follow-up and for periods individuals spent at high CVD risk according to:
  i. total cholesterol (TC) >6.2 mmol/L (>240 mg/dl)
  ii. triglyceride (TG) >2.3 mmol/L (>124 mg/dl)
  iii. hypertension
  iv. previous MI
  v. diabetes
  vi. age >50 years
  vii. predicted 10-year Framingham CVD risk score >10%
- Poisson regression assessed whether rates of initiation were higher in men than women, after adjustment for potential confounders

Results

Baseline Characteristics of Women and Men in D:A:D

Demographic Factors		Men, N (%)	Women, N (%)	p-value
Number		36,664 (100)	13,039 (100)	
Mode of infection	MSM	21,809 (59.5)		
	IDU	5187 (14.2)	2428 (18.6)	
	Heterosexual	7199 (19.6)	8999 (69.0)	
	Other	2469 (6.7)	1612 (12.4)	0.0001
White Race		19,335 (52.7)	5825 (44.7)	
Age (years)	Median (IQR)	39 (33, 46)	34 (29, 40)	0.0001
BMI (kg/m^2)	<18	875 (2.4)	716 (5.5)	
	$\geq$18, $\leq$26	2444 (66.7)	7808 (59.9)	
	>26, $\leq$30	4733 (12.9)	1391 (10.7)	
	>30	1262 (3.4)	934 (7.2)	
	Not known	5351 (14.6)	2190 (16.8)	0.0001
Smoking	Current	13,669 (37.3)	3821 (29.3)	
	Ex-	6497 (17.7)	1810 (13.9)	
	Never	8285 (22.6)	4834 (37.1)	
	Not known	8213 (22.4)	2574 (19.7)	0.0001

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Follow-up Time (PYRS) Spent at High CVD Risk, Women and Men in D:A:D

High CVD risk group:	Men, N (%)	Women, N (%)
Total	269,706 (100.0)	97,065 (100.0)
Total cholesterol >6.2 mmol/L (> 240 mg/dl)	39,098 (14.5)	12,920 (13.3)
Triglycerides > 3.2 mmol/L (> 124 mg/dl)	81,277 (30.1)	14,863 (15.3)
Hypertension	58,582 (21.7)	14,544 (15.0)
Previous MI	3171 (1.2)	274 (0.3)
Diabetes	13,818 (5.1)	3269 (3.4)
Age > 50 years	77,859 (28.9)	14,841 (15.3)
CVD risk score > 10 %	69,067 (25.6)	3985 (4.1)

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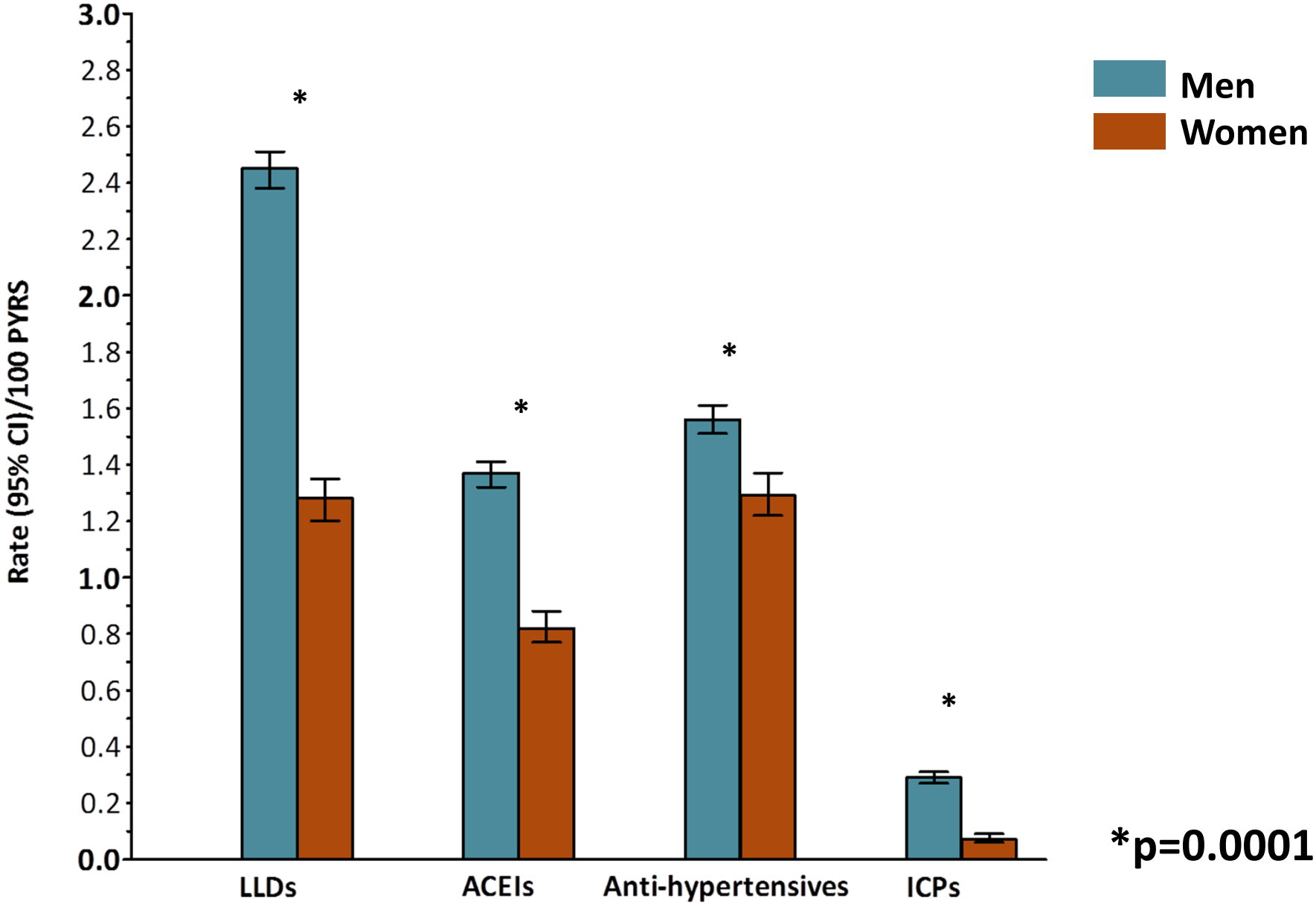
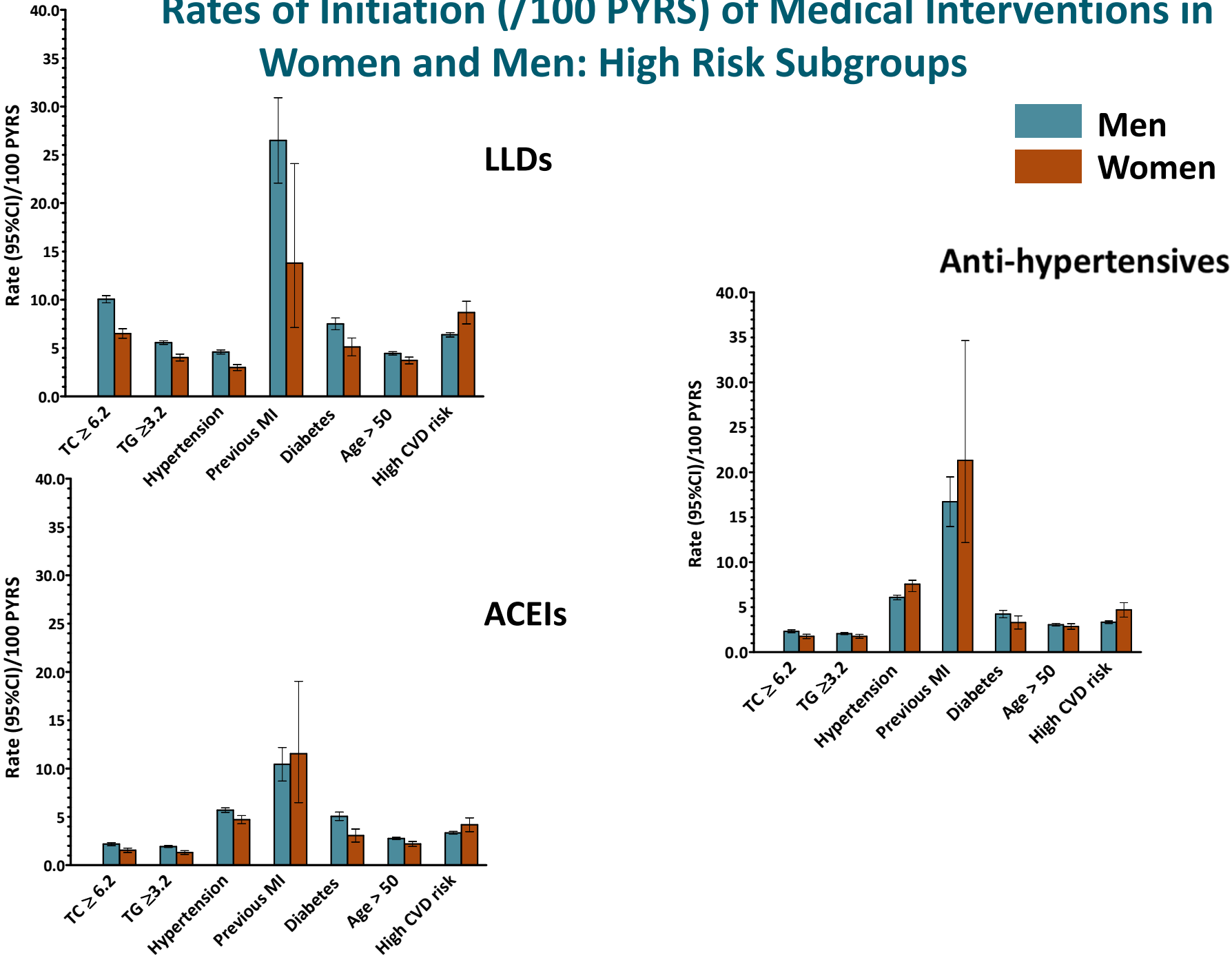
Rates of Initiation (/100 PYRS) of Interventions in Women and Men, Total Follow-up Period



Rates of Initiation (/100 PYRS) of Medical Interventions in Women and Men: High Risk Subgroups



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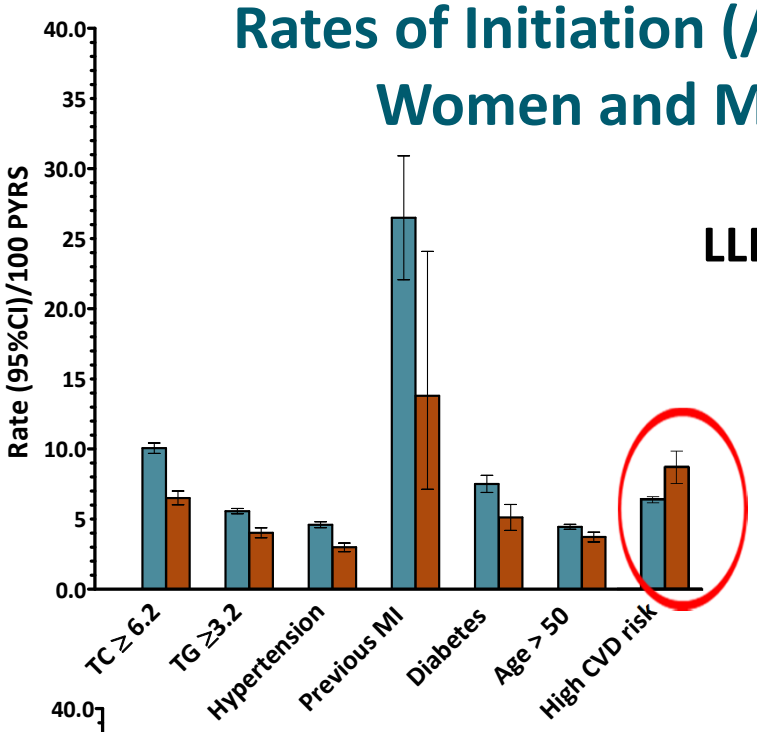
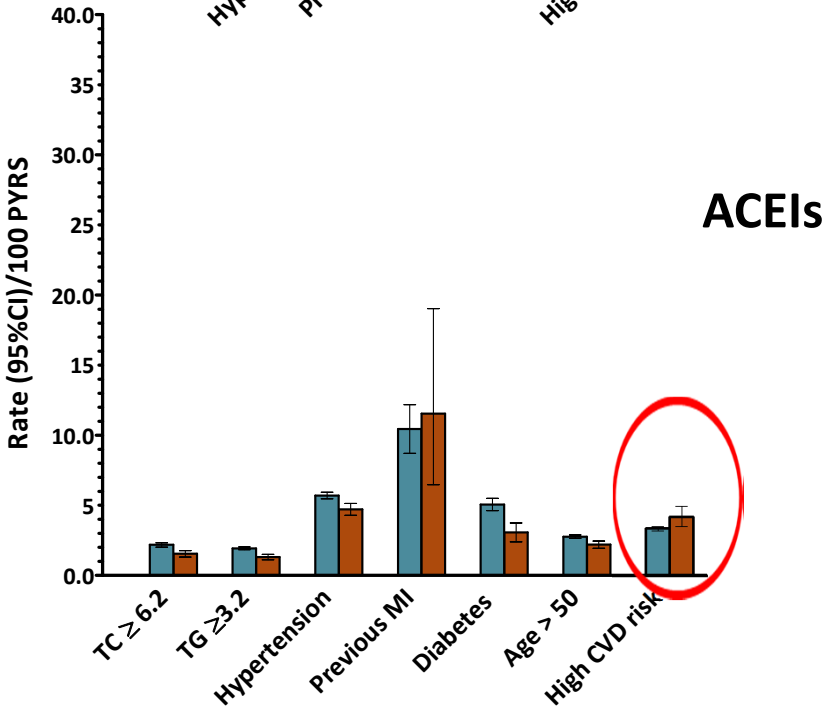
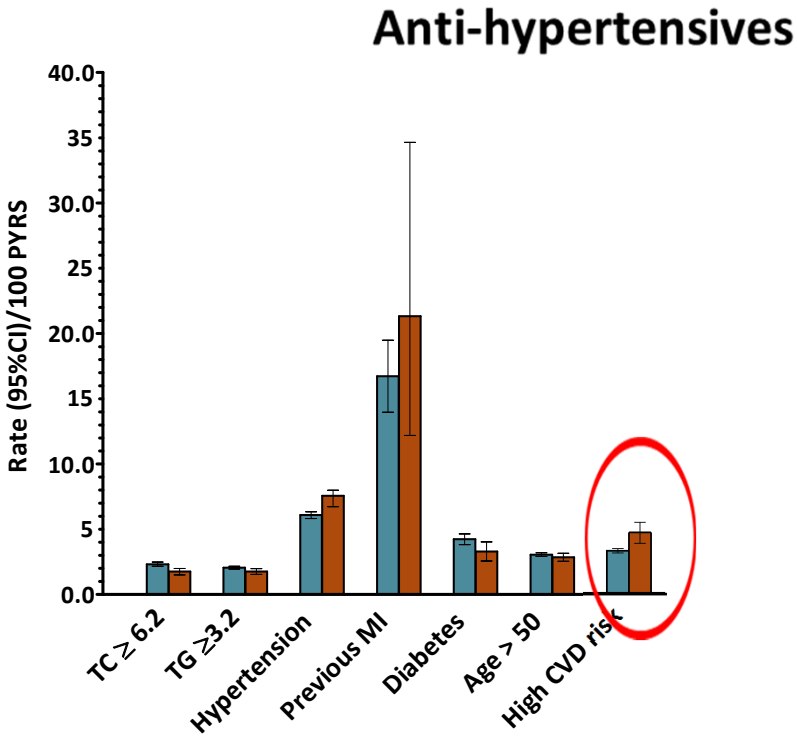
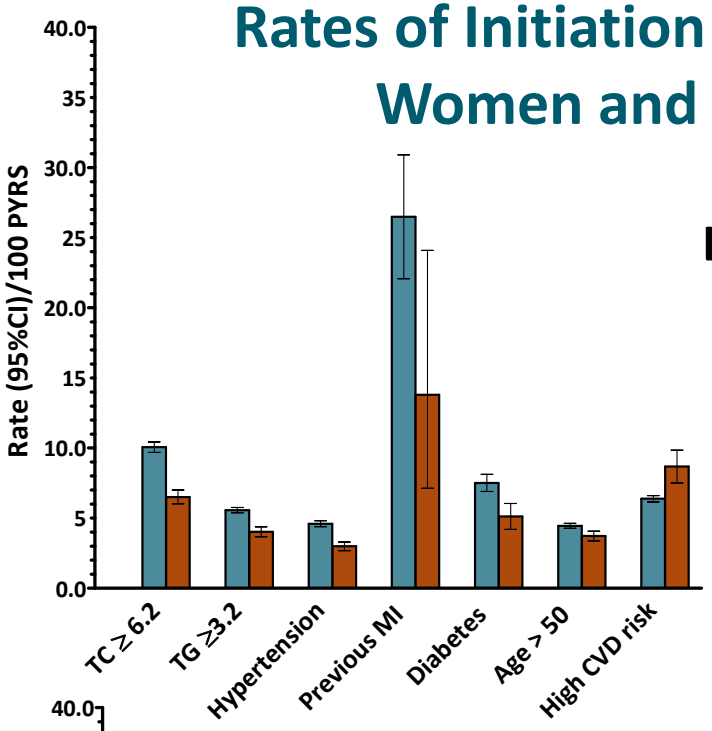
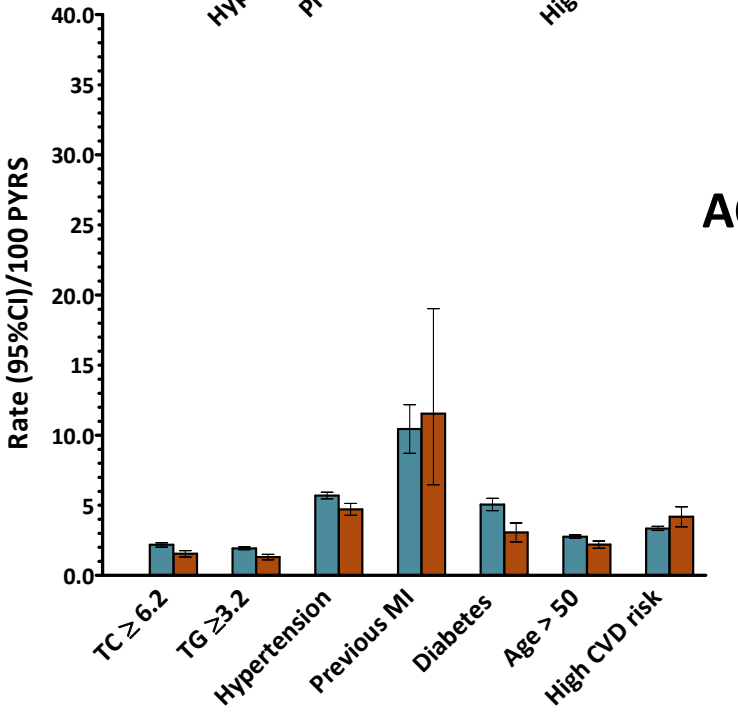


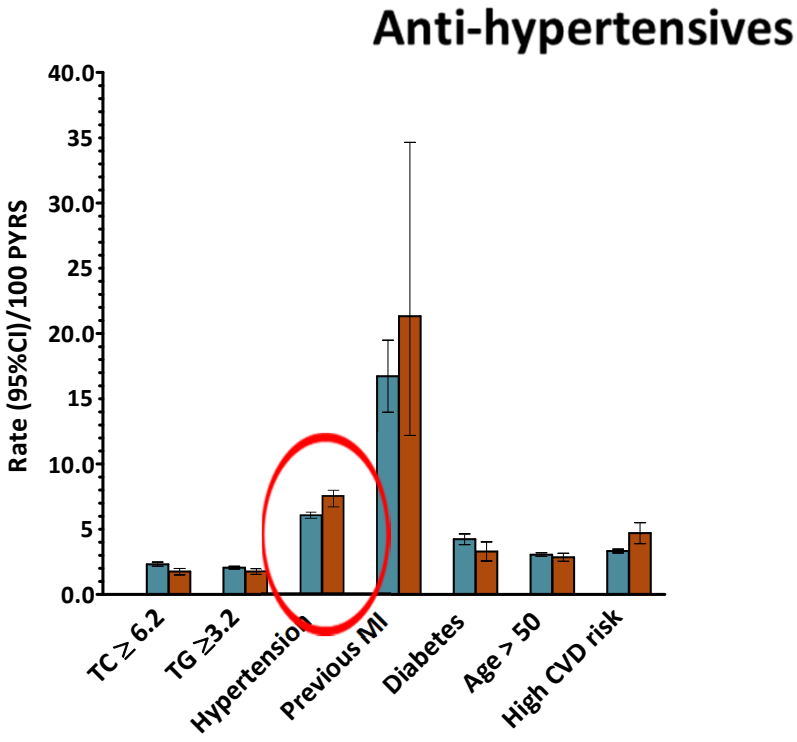




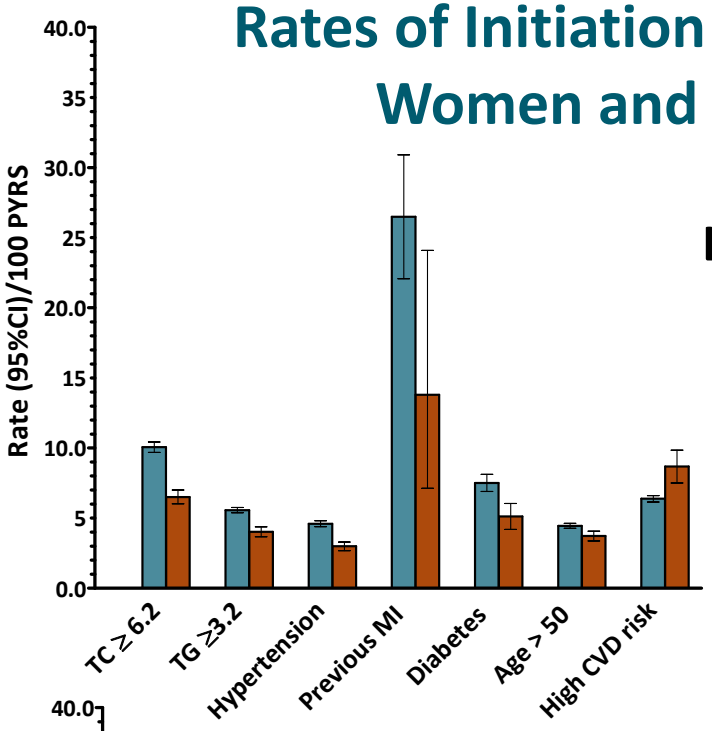
Rates of Initiation (/100 PYRS) of Medical Interventions in Women and Men: High Risk Subgroups

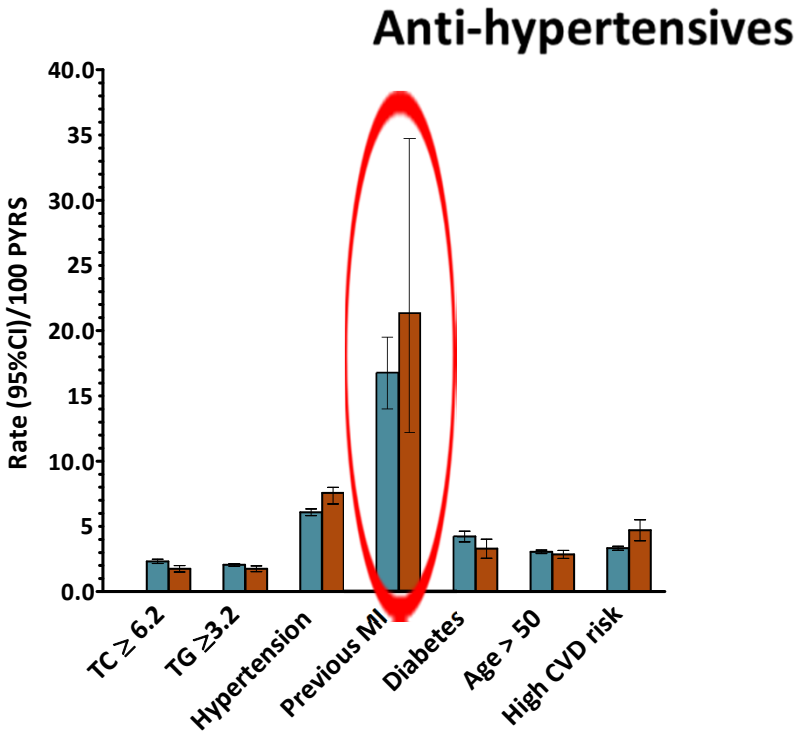


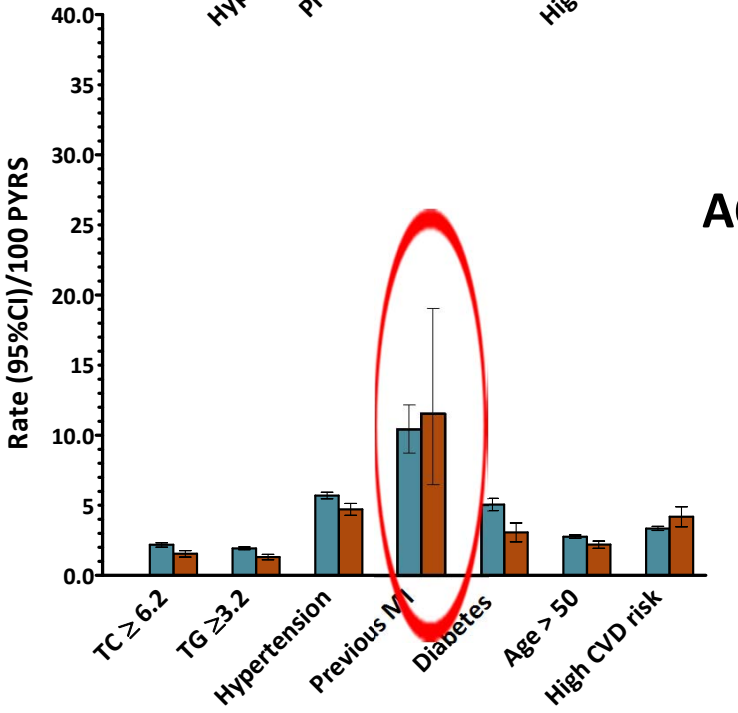




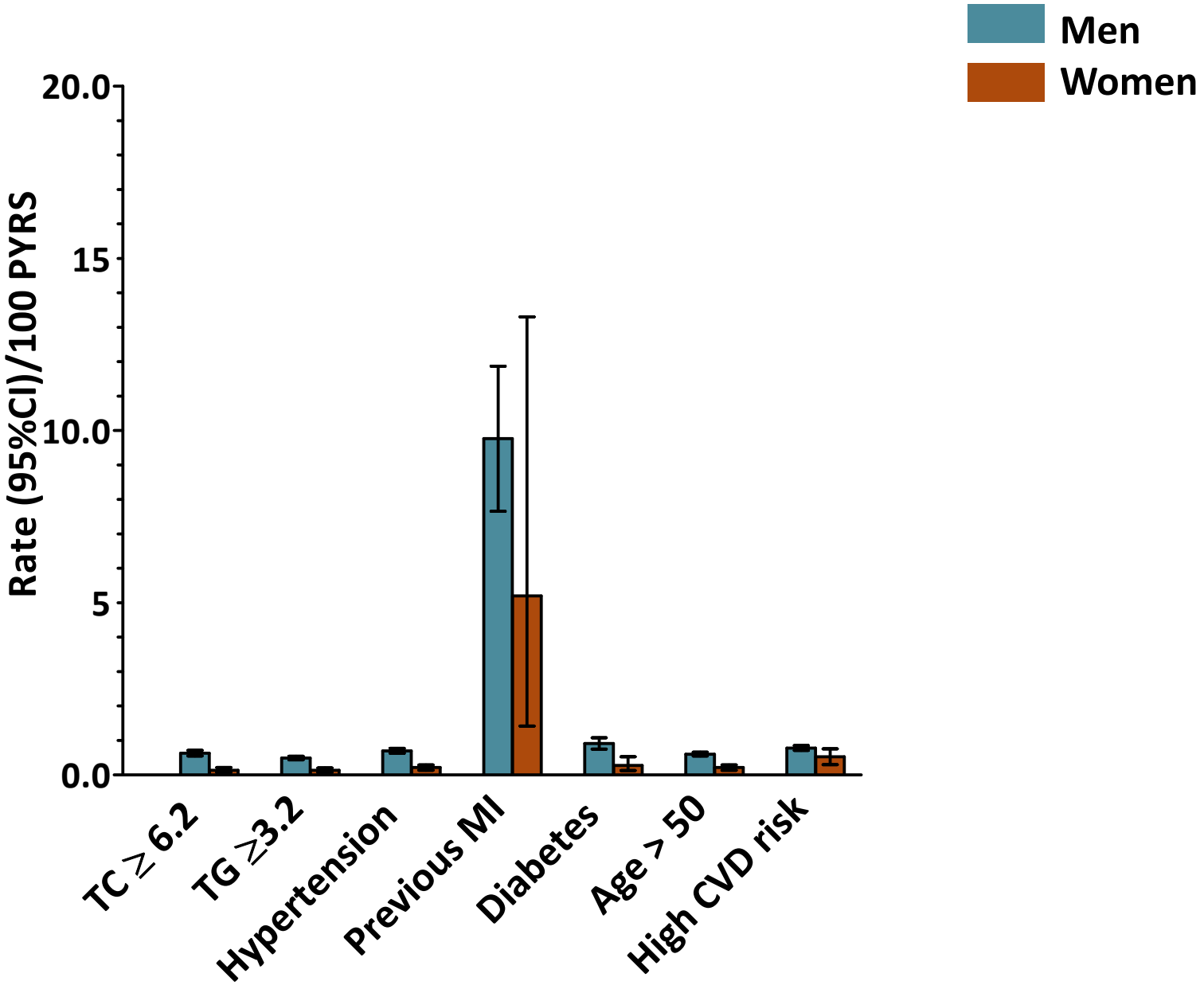
Rates of Initiation (/100 PYRS) of Medical Interventions in Women and Men: High Risk Subgroups



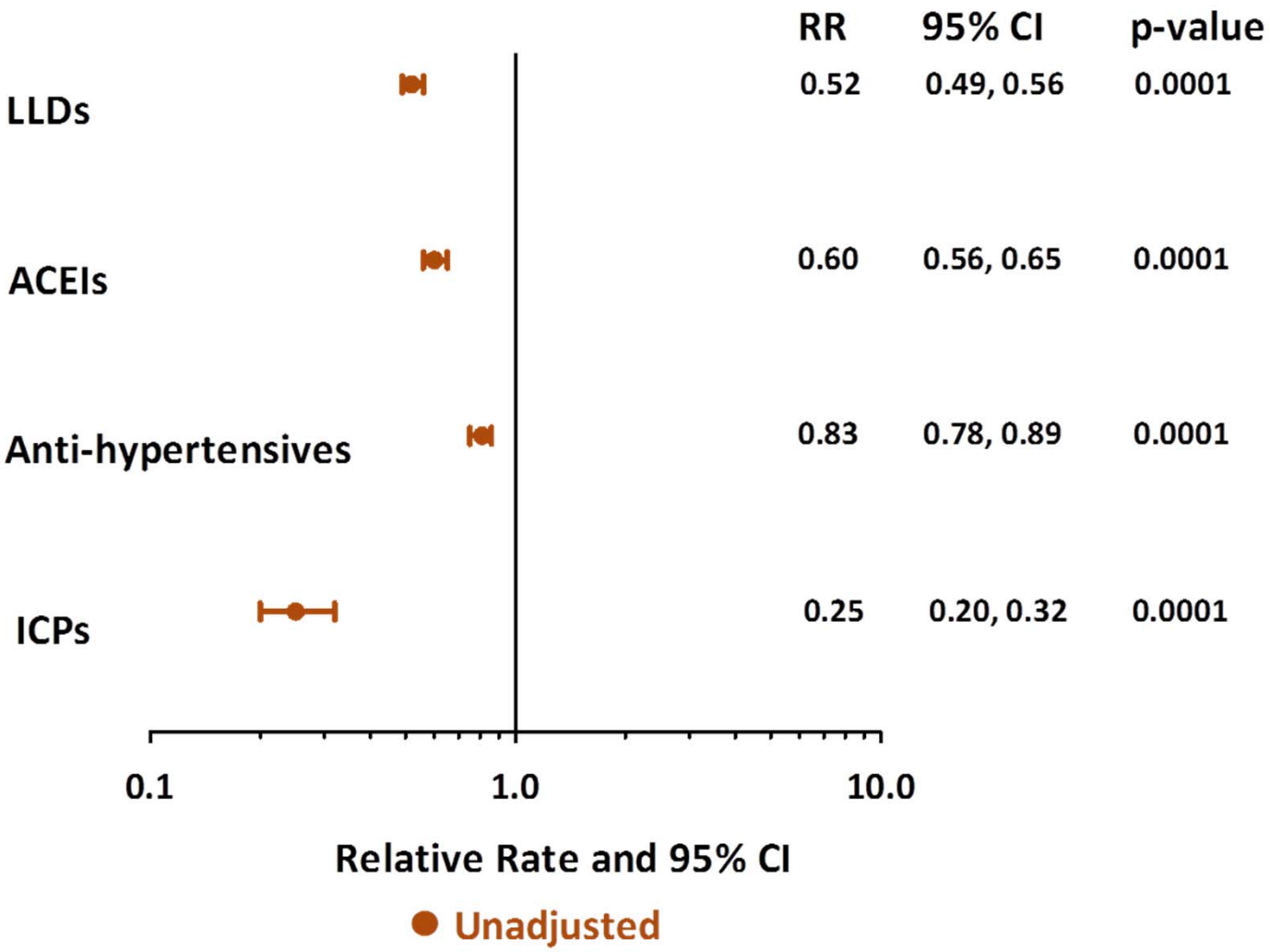




Rates of Initiation (/100 PYRS) of Invasive Interventions in Women and Men: High Risk Subgroups



Relative Rate (RR) of Receipt of Interventions in Women Compared to Men



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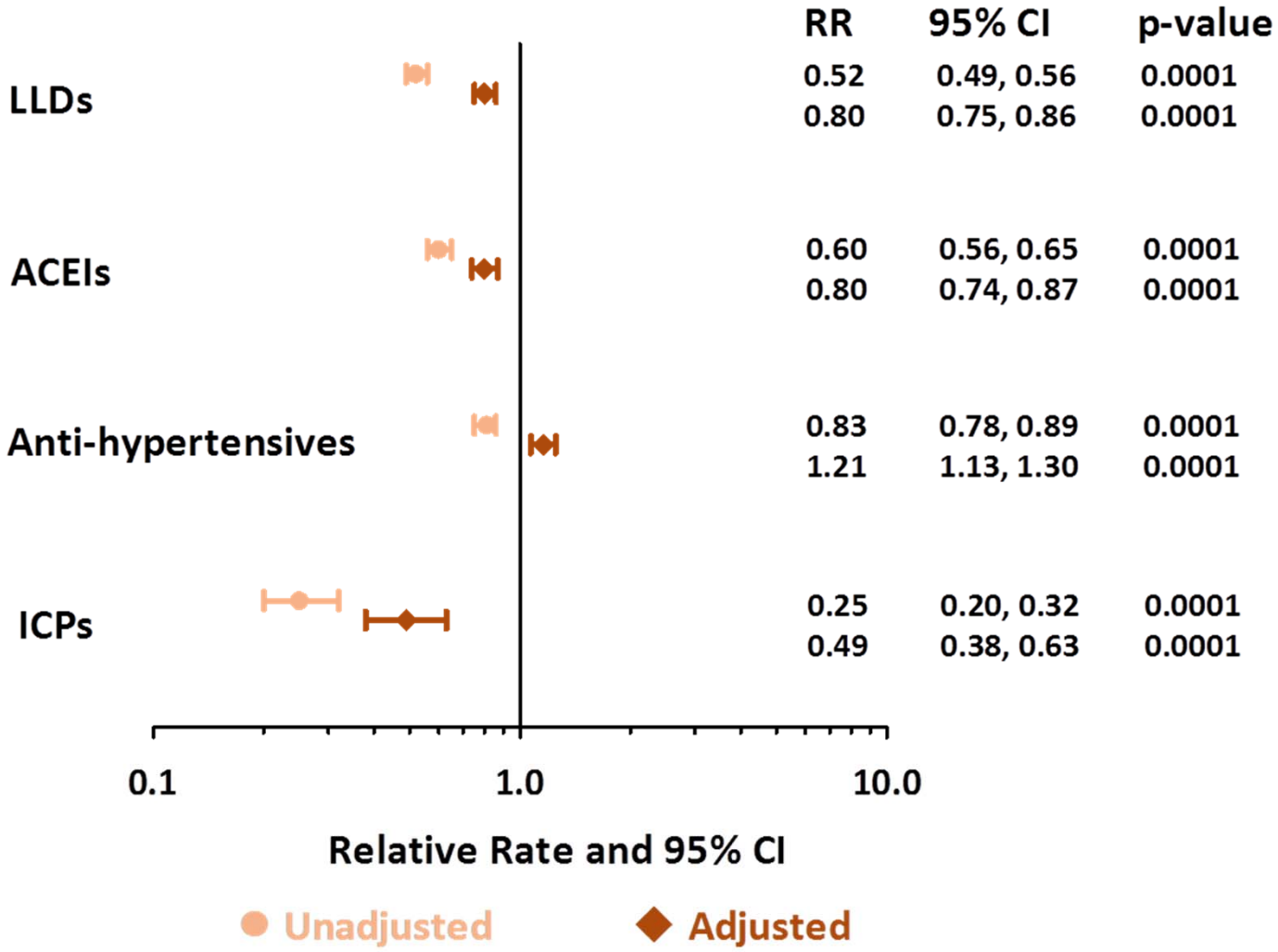

*Adjustment for age, calendar year, body mass index, total cholesterol, triglycerides, hypertension, previous MI, diabetes and moderate/high predicted 10-year CVD Framingham risk score

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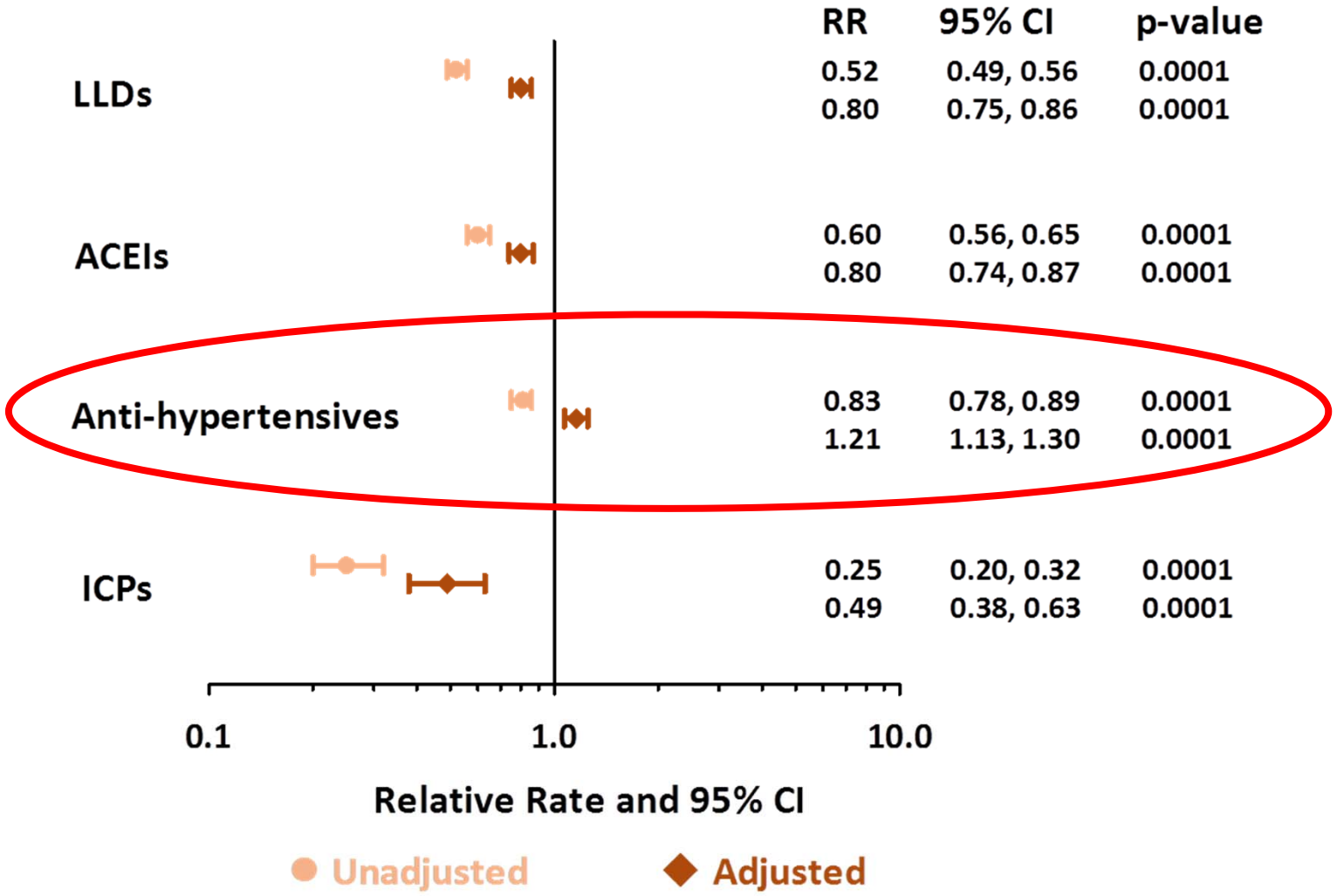

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Sensitivity Analyses

- Potential residual confounding:
  Additional adjustment for the following variables did not change the gender associations:

  - Race, smoking status, AIDS, CVD family history, stroke
  - TC, TG, systolic/diastolic blood pressure as continuous covariates

- Associations between female gender and probability of receiving any intervention did not change when excluding those with a mode of HIV-acquisition other than heterosexual sex

Strengths and Limitations

- Hard to determine the exact reasons for the gender associations seen, though an observational study is the best option
- Large, heterogeneous cohort study with substantial follow-up time and centrally validated endpoints which is suitable when investigating risk factors and interventions
- Preventive CVD-interventions such as advice on exercise and smoking are not captured in our dataset, and some individuals may not accept interventions offered
- Potential under- or delayed-ascertainment of the receipt of CVD-interventions

Summary

- The initiation rates of CVD-related interventions were lower among women than men for the total follow-up period

- Initiation rates of CVD-related interventions for time spent at high CVD risk were lower in women than for men for most high risk subgroups

- After adjustment for potential confounders, women were less likely to receive interventions than men, with the exception of anti-hypertensive drugs

Perspectives

- Actions should be taken to ensure that both women and men are sufficiently monitored for CVD and, if required, receive appropriate CVD-related interventions

- Guidelines for the management of CVD in HIV+ individuals generally focus on moderate/high risk subgroups; women may be less frequently monitored as they are more likely to have low CVD risk

- Further investigation into potential differences in monitoring of CVD risk factors between women and men are warranted

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